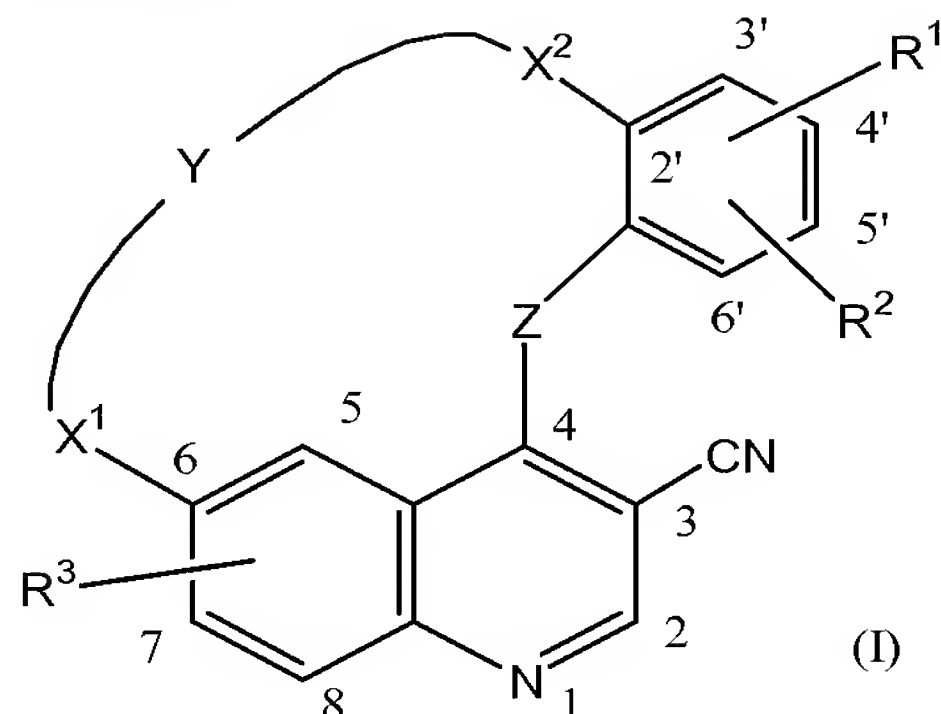


-56-

# Claims

1. A compound having the formula



5 the *N*-oxide forms, the pharmaceutically acceptable addition salts and the stereochemically isomeric forms thereof, wherein

Z represents O, NH or S;

Y represents -C<sub>3-9</sub>alkyl-, -C<sub>3-9</sub>alkenyl-, -C<sub>1-5</sub>alkyl-oxy-C<sub>1-5</sub>alkyl-,

10 -C<sub>1-5</sub>alkyl-NR<sup>12</sup>-C<sub>1-5</sub>alkyl-, -C<sub>1-5</sub>alkyl-NR<sup>13</sup>-CO-C<sub>1-5</sub>alkyl-,  
-C<sub>1-5</sub>alkyl-CO-NR<sup>14</sup>-C<sub>1-5</sub>alkyl-, -C<sub>1-6</sub>alkyl-CO-NH-, -C<sub>1-6</sub>alkyl-NH-CO-,  
-CO-NH-C<sub>1-6</sub>alkyl-, -NH-CO-C<sub>1-6</sub>alkyl-, -CO-C<sub>1-7</sub>alkyl-, -C<sub>1-7</sub>alkyl-CO-,  
C<sub>1-6</sub>alkyl-CO-C<sub>1-6</sub>alkyl, -C<sub>1-2</sub>alkyl-NH-CO-CH<sub>2</sub>R<sup>15</sup>-NH-;

X<sup>1</sup> represents a direct bond, O, -O-C<sub>1-2</sub>alkyl-, CO, -CO- C<sub>1-2</sub>alkyl-, NR<sup>10</sup>,  
15 -NR<sup>10</sup>-C<sub>1-2</sub>alkyl-, NR<sup>16</sup>-CO-, NR<sup>16</sup>-CO-C<sub>1-2</sub>alkyl, -O-N=CH- or C<sub>1-2</sub>alkyl;

X<sup>2</sup> represents a direct bond, O, -O-C<sub>1-2</sub>alkyl-, CO, -CO- C<sub>1-2</sub>alkyl-, NR<sup>11</sup>,  
NR<sup>11</sup>-C<sub>1-2</sub>alkyl-, NR<sup>17</sup>-CO-, NR<sup>17</sup>-CO-C<sub>1-2</sub>alkyl, Het<sup>20</sup>-C<sub>1-2</sub>alkyl, -O-N=CH- or C<sub>1-2</sub>alkyl;

R<sup>1</sup> represents hydrogen, cyano, halo, hydroxy, formyl, C<sub>1-6</sub>alkoxy-, C<sub>1-6</sub>alkyl-,  
20 C<sub>1-6</sub>alkoxy- substituted with halo,  
C<sub>1-4</sub>alkyl substituted with one or where possible two or more substituents selected  
from hydroxy or halo;

R<sup>2</sup> represents hydrogen, cyano, halo, hydroxy, hydroxycarbonyl-, Het<sup>16</sup>-carbonyl-,  
C<sub>1-4</sub>alkyloxycarbonyl-, C<sub>1-4</sub>alkylcarbonyl-, aminocarbonyl-,  
25 mono-or di(C<sub>1-4</sub>alkyl)aminocarbonyl-, Het<sup>1</sup>, formyl, C<sub>1-4</sub>alkyl-, C<sub>2-6</sub>alkynyl-,  
C<sub>3-6</sub>cycloalkyl-, C<sub>3-6</sub>cycloalkyloxy-, C<sub>1-6</sub>alkoxy-, Ar<sup>5</sup>, Ar<sup>1</sup>-oxy-, dihydroxyborane ,  
C<sub>1-6</sub>alkoxy- substituted with halo,  
C<sub>1-4</sub>alkyl substituted with one or where possible two or more substituents selected  
from halo, hydroxy or NR<sup>4</sup>R<sup>5</sup>,

-57-

- C<sub>1-4</sub>alkylcarbonyl- wherein said C<sub>1-4</sub>alkyl is optionally substituted with one or where possible two or more substituents selected from hydroxy or C<sub>1-4</sub>alkyl-oxy-;
- R<sup>3</sup> represents hydrogen, hydroxy, Ar<sup>3</sup>-oxy, Ar<sup>4</sup>-C<sub>1-4</sub>alkyloxy-, C<sub>1-4</sub>alkyloxy-,  
5 C<sub>2-4</sub>alkenyloxy- optionally substituted with Het<sup>12</sup> or R<sup>3</sup> represents C<sub>1-4</sub>alkyloxy substituted with one or where possible two or more substituents selected from C<sub>1-4</sub>alkyloxy-, hydroxy, halo, Het<sup>2</sup>-, -NR<sup>6</sup>R<sup>7</sup>-, -carbonyl- NR<sup>8</sup>R<sup>9</sup> or Het<sup>3</sup>-carbonyl-;
- R<sup>4</sup> and R<sup>5</sup> are each independently selected from hydrogen or C<sub>1-4</sub>alkyl;
- R<sup>6</sup> and R<sup>7</sup> are each independently selected from hydrogen, C<sub>1-4</sub>alkyl, Het<sup>8</sup>,  
10 aminosulfonyl-, mono- or di (C<sub>1-4</sub>alkyl)-aminosulfonyl, hydroxy-C<sub>1-4</sub>alkyl-, C<sub>1-4</sub>alkyl-oxy-C<sub>1-4</sub>alkyl-, hydroxycarbonyl-C<sub>1-4</sub>alkyl-, C<sub>3-6</sub>cycloalkyl, Het<sup>9</sup>-carbonyl-C<sub>1-4</sub>alkyl-, Het<sup>10</sup>-carbonyl-, polyhydroxy-C<sub>1-4</sub>alkyl-, Het<sup>11</sup>-C<sub>1-4</sub>alkyl- or Ar<sup>2</sup>-C<sub>1-4</sub>alkyl-;
- R<sup>8</sup> and R<sup>9</sup> are each independently selected from hydrogen, C<sub>1-4</sub>alkyl, C<sub>3-6</sub>cycloalkyl, Het<sup>4</sup>, hydroxy-C<sub>1-4</sub>alkyl-, C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyl- or polyhydroxy-C<sub>1-4</sub>alkyl-;  
15 R<sup>10</sup> represents hydrogen, C<sub>1-4</sub>alkyl, Het<sup>5</sup>, Het<sup>6</sup>-C<sub>1-4</sub>alkyl-, C<sub>2-4</sub>alkenylcarbonyl- optionally substituted with Het<sup>7</sup>-C<sub>1-4</sub>alkylaminocarbonyl-, C<sub>2-4</sub>alkenylsulfonyl-, C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyl- or phenyl optionally substituted with one or where possible two or more substituents selected from hydrogen, hydroxy, amino or C<sub>1-4</sub>alkyloxy-;
- 20 R<sup>11</sup> represents hydrogen, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkyl-oxy-carbonyl-, Het<sup>17</sup>, Het<sup>18</sup>-C<sub>1-4</sub>alkyl-, C<sub>2-4</sub>alkenylcarbonyl- optionally substituted with Het<sup>19</sup>-C<sub>1-4</sub>alkylaminocarbonyl-, C<sub>2-4</sub>alkenylsulfonyl-, C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyl- or phenyl optionally substituted with one or where possible two or more substituents selected from hydrogen, hydroxy, amino or C<sub>1-4</sub>alkyloxy-;
- 25 R<sup>12</sup> represents hydrogen, C<sub>1-4</sub>alkyl, Het<sup>13</sup>, Het<sup>14</sup>-C<sub>1-4</sub>alkyl- or phenyl optionally substituted with one or where possible two or more substituents selected from hydrogen, hydroxy, amino or C<sub>1-4</sub>alkyloxy-;
- R<sup>13</sup> and R<sup>14</sup> are each independently selected from hydrogen, C<sub>1-4</sub>alkyl, Het<sup>15</sup>-C<sub>1-4</sub>alkyl- or C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyl-;
- 30 R<sup>15</sup> represents hydrogen or C<sub>1-4</sub>alkyl optionally substituted with phenyl, indolyl, methylsulfide, hydroxy, thiol, hydroxyphenyl, aminocarbonyl, hydroxycarbonyl, amine, imidazolyl or guanidino;
- R<sup>16</sup> and R<sup>17</sup> are each independently selected from hydrogen, C<sub>1-4</sub>alkyl, Het<sup>21</sup>-C<sub>1-4</sub>alkyl or C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyl-;
- 35 Het<sup>1</sup> represents a heterocycle selected from piperidinyl, morpholinyl, piperazinyl, furanyl, pyrazolyl, dioxolanyl, thiazolyl, oxazolyl, imidazolyl, isoxazolyl, oxadiazolyl, pyridinyl or pyrrolidinyl wherein said Het<sup>1</sup> is optionally substituted

-58-

amino, C<sub>1-4</sub>alkyl, hydroxy-C<sub>1-4</sub>alkyl-, phenyl, phenyl-C<sub>1-4</sub>alkyl-,  
C<sub>1-4</sub>alkyl-oxy-C<sub>1-4</sub>alkyl- mono- or di(C<sub>1-4</sub>alkyl)amino- or amino-carbonyl-;  
Het<sup>2</sup> represents a heterocycle selected from morpholinyl, piperazinyl, piperidinyl,  
pyrrolidinyl, thiomorpholinyl or dithianyl wherein said Het<sup>2</sup> is optionally  
5 substituted with one or where possible two or more substituents selected from  
hydroxy, halo, amino, C<sub>1-4</sub>alkyl-, hydroxy-C<sub>1-4</sub>alkyl-, C<sub>1-4</sub>alkyl-oxy-C<sub>1-4</sub>alkyl-,  
hydroxy-C<sub>1-4</sub>alkyl-oxy-C<sub>1-4</sub>alkyl-, mono- or di(C<sub>1-4</sub>alkyl)amino-,  
mono- or di(C<sub>1-4</sub>alkyl)amino-C<sub>1-4</sub>alkyl-, aminoC<sub>1-4</sub>alkyl-,  
mono- or di(C<sub>1-4</sub>alkyl)amino-sulfonyl-, aminosulfonyl-;  
10 Het<sup>3</sup>, Het<sup>4</sup> and Het<sup>8</sup> each independently represent a heterocycle selected from  
morpholinyl, piperazinyl, piperidinyl, furanyl, pyrazolyl, dioxolanyl, thiazolyl,  
oxazolyl, imidazolyl, isoxazolyl, oxadiazolyl, pyridinyl or pyrrolidinyl wherein  
said Het<sup>3</sup>, Het<sup>4</sup> or Het<sup>8</sup> is optionally substituted with one or where possible two or  
more substituents selected from hydroxy-, amino-, C<sub>1-4</sub>alkyl-,  
15 C<sub>3-6</sub>cycloalkyl-C<sub>1-4</sub>alkyl-, aminosulfonyl-, mono- or di(C<sub>1-4</sub>alkyl)aminosulfonyl or  
amino-C<sub>1-4</sub>alkyl-;  
Het<sup>5</sup> represent a heterocycle selected from pyrrolidinyl or piperidinyl wherein said Het<sup>5</sup>  
optionally substituted with one or where possible two or more substituents selected  
from C<sub>1-4</sub>alkyl, C<sub>3-6</sub>cycloalkyl, hydroxy-C<sub>1-4</sub>alkyl-, C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyl or  
20 polyhydroxy-C<sub>1-4</sub>alkyl-;  
Het<sup>6</sup> and Het<sup>7</sup> each independently represent a heterocycle selected from morpholinyl,  
pyrrolidinyl, piperazinyl or piperidinyl wherein said Het<sup>6</sup> and Het<sup>7</sup> are optionally  
substituted with one or where possible two or more substituents selected from  
C<sub>1-4</sub>alkyl, C<sub>3-6</sub>cycloalkyl, hydroxy-C<sub>1-4</sub>alkyl-, C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyl or  
25 polyhydroxy-C<sub>1-4</sub>alkyl-;  
Het<sup>9</sup> and Het<sup>10</sup> each independently represent a heterocycle selected from furanyl,  
piperidinyl, morpholinyl, piperazinyl, pyrazolyl, dioxolanyl, thiazolyl, oxazolyl,  
imidazolyl, isoxazolyl, oxadiazolyl, pyridinyl or pyrrolidinyl wherein said Het<sup>9</sup> or  
Het<sup>10</sup> is optionally substituted C<sub>1-4</sub>alkyl, C<sub>3-6</sub>cycloalkyl-C<sub>1-4</sub>alkyl- or  
30 amino-C<sub>1-4</sub>alkyl-;

Het<sup>11</sup> represents a heterocycle selected from indolyl or  ;

Het<sup>12</sup> represents a heterocycle selected from morpholinyl, piperazinyl, piperidinyl,  
pyrrolidinyl, thiomorpholinyl or dithianyl wherein said Het<sup>12</sup> is optionally  
substituted with one or where possible two or more substituents selected from  
35 hydroxy, halo, amino, C<sub>1-4</sub>alkyl-, hydroxy-C<sub>1-4</sub>alkyl-, C<sub>1-4</sub>alkyl-oxy-C<sub>1-4</sub>alkyl-,

-59-

hydroxy-C<sub>1-4</sub>alkyl-oxy-C<sub>1-4</sub>alkyl-, mono- or di(C<sub>1-4</sub>alkyl)amino- or  
mono- or di(C<sub>1-4</sub>alkyl)amino-C<sub>1-4</sub>alkyl-;

Het<sup>13</sup> represent a heterocycle selected from pyrrolidinyl or piperidinyl wherein said  
Het<sup>13</sup> is optionally substituted with one or where possible two or more substituents  
5 selected from C<sub>1-4</sub>alkyl, C<sub>3-6</sub>cycloalkyl, hydroxy-C<sub>1-4</sub>alkyl-, C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyl  
or polyhydroxy-C<sub>1-4</sub>alkyl-;

Het<sup>14</sup> represent a heterocycle selected from morpholinyl, pyrrolidinyl, piperazinyl or  
piperidinyl wherein said Het<sup>14</sup> is optionally substituted with one or where possible  
two or more substituents selected from C<sub>1-4</sub>alkyl, C<sub>3-6</sub>cycloalkyl,  
10 hydroxy-C<sub>1-4</sub>alkyl-, C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyl or polyhydroxy-C<sub>1-4</sub>alkyl-;

Het<sup>15</sup> and Het<sup>21</sup> each independently represent a heterocycle selected from morpholinyl,  
pyrrolidinyl, piperazinyl or piperidinyl wherein said heterocycles are optionally  
substituted with one or where possible two or more substituents selected from C<sub>1-4</sub>  
4alkyl, C<sub>3-6</sub>cycloalkyl, hydroxy-C<sub>1-4</sub>alkyl-,

15 C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyl or polyhydroxy-C<sub>1-4</sub>alkyl-;

Het<sup>16</sup> represent a heterocycle selected from morpholinyl, pyrrolidinyl, piperazinyl,  
1,3,2-dioxaborolane or piperidinyl wherein said heterocycle is optionally  
substituted with one or more substituents selected from C<sub>1-4</sub>alkyl; and

Het<sup>17</sup> represent a heterocycle selected from pyrrolidinyl or piperidinyl wherein said  
20 Het<sup>17</sup> is optionally substituted with one or where possible two or more substituents  
selected from C<sub>1-4</sub>alkyl, C<sub>3-6</sub>cycloalkyl, hydroxy-C<sub>1-4</sub>alkyl-, C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyl  
or polyhydroxy-C<sub>1-4</sub>alkyl-;

Het<sup>18</sup> and Het<sup>19</sup> each independently represent a heterocycle selected from morpholinyl,  
pyrrolidinyl, piperazinyl or piperidinyl wherein said Het<sup>18</sup> and Het<sup>19</sup> are optionally  
25 substituted with one or where possible two or more substituents selected from  
C<sub>1-4</sub>alkyl, C<sub>3-6</sub>cycloalkyl, hydroxy-C<sub>1-4</sub>alkyl-, C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyl or  
polyhydroxy-C<sub>1-4</sub>alkyl-;

Het<sup>20</sup> represents a heterocycle selected from pyrrolidinyl, 2-pyrrolidinyl, piperidinyl,  
piperazinyl, morpholinyl, imidazolyl or pyrazolidinyl wherein said Het<sup>20</sup> is  
30 optionally substituted with one or where possible two or more substituents selected  
from C<sub>1-4</sub>alkyl, C<sub>3-6</sub>cycloalkyl, hydroxy-C<sub>1-4</sub>alkyl-, C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyl or  
polyhydroxy-C<sub>1-4</sub>alkyl-; and

Ar<sup>1</sup>, Ar<sup>2</sup>, Ar<sup>3</sup>, Ar<sup>4</sup> and Ar<sup>5</sup> each independently represent phenyl optionally substituted  
with cyano, C<sub>1-4</sub>alkylsulfonyl-, C<sub>1-4</sub>alkylsulfonylamino-, aminosulfonylamino-,  
35 hydroxy-C<sub>1-4</sub>alkyl, aminosulfonyl-, hydroxy-, C<sub>1-4</sub>alkyloxy- or C<sub>1-4</sub>alkyl.

2. A compound according to claim 1 wherein;

-60-

Another group of compounds consists of those compounds of formula (I) wherein one or more of the following restrictions apply:

Z represents NH;

Y represents -C<sub>3-9</sub>alkyl-, -C<sub>2-9</sub>alkenyl-, -C<sub>1-5</sub>alkyl-oxy-C<sub>1-5</sub>alkyl-,

5        -C<sub>1-5</sub>alkyl-NR<sup>12</sup>-C<sub>1-5</sub>alkyl-, -C<sub>1-5</sub>alkyl-NR<sup>13</sup>-CO-C<sub>1-5</sub>alkyl-, -C<sub>1-6</sub>alkyl-NH-CO-,  
      -CO-C<sub>1-7</sub>alkyl-, -C<sub>1-7</sub>alkyl-CO- or C<sub>1-6</sub>alkyl-CO-C<sub>1-6</sub>alkyl;

X<sup>1</sup> represents O, -O-C<sub>1-2</sub>alkyl-, -O-N=CH-, NR<sup>16</sup>-CO, -NR<sup>16</sup>-CO-C<sub>1-2</sub>alkyl-, NR<sup>10</sup> or  
      -NR<sup>10</sup>-C<sub>1-2</sub>alkyl-; in a particular embodiment X<sup>1</sup> represents -O-, -O-CH<sub>2</sub>-, NR<sup>10</sup> or  
      -NR<sup>10</sup>-C<sub>1-2</sub>alkyl-;

10    X<sup>2</sup> represents a direct bond, O, -O-C<sub>1-2</sub>alkyl-, -O-N=CH-, Het<sup>20</sup>-C<sub>1-2</sub>alkyl, C<sub>1-2</sub>alkyl,  
      NR<sup>17</sup>-CO, -NR<sup>17</sup>-CO-C<sub>1-2</sub>alkyl-, NR<sup>11</sup> or NR<sup>11</sup>-C<sub>1-2</sub>alkyl-; in a particular  
      embodiment X<sup>2</sup> represents a direct bond, -O-N=CH-, -NR<sup>11</sup>-C<sub>1-2</sub>alkyl-,  
      -NR<sup>11</sup>-CH<sub>2</sub>-, Het<sup>20</sup>-C<sub>1-2</sub>alkyl, NR<sup>17</sup>-CO, -NR<sup>17</sup>-CO-C<sub>1-2</sub>alkyl- -C<sub>1-2</sub>alkyl-,  
      -O-C<sub>1-2</sub>alkyl, -O- or -O-CH<sub>2</sub>-;

15    R<sup>1</sup> represents hydrogen, cyano, halo or hydroxy, preferably halo;

R<sup>2</sup> represents hydrogen, cyano, halo, hydroxy, hydroxycarbonyl-, C<sub>1-4</sub>alkyloxycarbonyl-,  
      Het<sup>16</sup>-carbonyl-, C<sub>2-6</sub>alkynyl-, Ar<sup>5</sup> or Het<sup>1</sup>;

In a further embodiment R<sup>2</sup> represents hydrogen, cyano, halo, hydroxy,  
      C<sub>2-6</sub>alkynyl- or Het<sup>1</sup>;

20    R<sup>3</sup> represents hydrogen, hydroxy, C<sub>1-4</sub>alkyloxy-, Ar<sup>4</sup>-C<sub>1-4</sub>alkyloxy or R<sup>3</sup> represents  
      C<sub>1-4</sub>alkyloxy substituted with one or where possible two or more substituents  
      selected from C<sub>1-4</sub>alkyloxy- or Het<sup>2</sup>-;

R<sup>10</sup> represents hydrogen, C<sub>1-4</sub>alkyl- or C<sub>1-4</sub>alkyl-oxy-carbonyl-;

R<sup>11</sup> represents hydrogen, C<sub>1-4</sub>alkyl- or C<sub>1-4</sub>alkyl-oxy-carbonyl-;

25    R<sup>12</sup> represents Het<sup>14</sup>-C<sub>1-4</sub>alkyl, in particular morpholinyl-C<sub>1-4</sub>alkyl;

R<sup>16</sup> represents hydrogen, C<sub>1-4</sub>alkyl-, Het<sup>21</sup>-C<sub>1-4</sub>alkyl or C<sub>1-4</sub>alkyl-oxy-C<sub>1-4</sub>alkyl; in  
      particular R<sup>16</sup> represents hydrogen or C<sub>1-4</sub>alkyl;

R<sup>17</sup> represents hydrogen, C<sub>1-4</sub>alkyl-, Het<sup>21</sup>-C<sub>1-4</sub>alkyl or C<sub>1-4</sub>alkyl-oxy-C<sub>1-4</sub>alkyl; in  
      particular R<sup>16</sup> represents hydrogen or C<sub>1-4</sub>alkyl;

30    Het<sup>1</sup> represents thiazolyl optionally substituted amino, C<sub>1-4</sub>alkyl, hydroxy-C<sub>1-4</sub>alkyl-,  
      phenyl, phenyl-C<sub>1-4</sub>alkyl-, C<sub>1-4</sub>alkyl-oxy-C<sub>1-4</sub>alkyl- mono- or di(C<sub>1-4</sub>alkyl)amino-  
      or amino-carbonyl-;

Het<sup>2</sup> represents a heterocycle selected from morpholinyl, piperazinyl, piperidinyl or  
      pyrrolidinyl wherein said Het<sup>2</sup> is optionally substituted with one or where possible  
35    two or more substituents selected from hydroxy, amino or C<sub>1-4</sub>alkyl-;

In a further embodiment Het<sup>2</sup> represents a heterocycle selected from morpholinyl  
      or piperidinyl optionally substituted with C<sub>1-4</sub>alkyl-, preferably methyl;

-61-

Het<sup>14</sup> represents a heterocycle selected from morpholinyl, piperazinyl, piperidinyl or pyrrolidinyl wherein said Het<sup>14</sup> is optionally substituted with one or where possible two or more substituents selected from hydroxy, amino or C<sub>1-4</sub>alkyl-;

Het<sup>16</sup> represents a heterocycle selected from piperidinyl, morpholinyl or pyrrolidinyl;

5 Het<sup>20</sup> represents a heterocycle selected from pyrrolidinyl, 2-pyrrolidinyl or piperidinyl;

Het<sup>21</sup> represents a heterocycle selected from morpholinyl, piperazinyl, piperidinyl or pyrrolidinyl wherein said Het<sup>21</sup> is optionally substituted with one or where possible two or more substituents selected from hydroxy, amino or C<sub>1-4</sub>alkyl-;

10 Ar<sup>4</sup> represents phenyl optionally substituted with cyano, hydroxy-, C<sub>1-4</sub>alkyloxy or C<sub>1-4</sub>alkyl;

Ar<sup>5</sup> represents phenyl optionally substituted with cyano, hydroxy, C<sub>1-4</sub>alkyloxy or C<sub>1-4</sub>alkyl.

3. A compound according to claim 1 wherein;

15 Z represents NH;

Y represents -C<sub>3-9</sub>alkyl-, -C<sub>1-5</sub>alkyl-NR<sup>12</sup>-C<sub>1-5</sub>alkyl-, -C<sub>1-5</sub>alkyl-NR<sup>13</sup>-CO-C<sub>1-5</sub>alkyl-, -C<sub>1-6</sub>alkyl-NH-CO- or -CO-NH -C<sub>1-6</sub>alkyl-;

X<sup>1</sup> represents a direct bond, NR<sup>10</sup>, -NR<sup>10</sup>-C<sub>1-2</sub>alkyl-, -NR<sup>10</sup>-CH<sub>2</sub>-, -C<sub>1-2</sub>alkyl-, -O-C<sub>1-2</sub>alkyl, -O- or -O-CH<sub>2</sub>-;

20 X<sup>2</sup> represents a-O-, NR<sup>11</sup>, NR<sup>17</sup>-CO, NR<sup>17</sup>-CO-C<sub>1-2</sub>alkyl or Het<sup>20</sup>-C<sub>1-2</sub>alkyl;

R<sup>1</sup> represents hydrogen or halo;

R<sup>2</sup> represents hydrogen, cyano, halo, hydroxycarbonyl-, C<sub>1-4</sub>alkyloxycarbonyl-, Het<sup>16</sup>-carbonyl- or Ar<sup>5</sup>;

25 R<sup>3</sup> represents hydrogen, hydroxy, C<sub>1-4</sub>alkyloxy-, Ar<sup>4</sup>-C<sub>1-4</sub>alkyloxy or R<sup>3</sup> represents C<sub>1-4</sub>alkyloxy substituted with one or where possible two or more substituents selected from C<sub>1-4</sub>alkyloxy- or Het<sup>2</sup>-;

R<sup>10</sup> represents hydrogen;

R<sup>11</sup> represents hydrogen, C<sub>1-4</sub>alkyl- or C<sub>1-4</sub>alkyl-oxy-carbonyl-;

R<sup>12</sup> represents Het<sup>14</sup>-C<sub>1-4</sub>alkyl, in particular morpholinyl-C<sub>1-4</sub>alkyl;

30 R<sup>13</sup> represents hydrogen;

R<sup>17</sup> represents hydrogen;

Het<sup>2</sup> represents a heterocycle selected from morpholinyl, piperazinyl, piperidinyl or pyrrolidinyl wherein said Het<sup>2</sup> is optionally substituted with one or where possible two or more substituents selected from hydroxy, amino or C<sub>1-4</sub>alkyl-;

35 In a further embodiment Het<sup>2</sup> represents a heterocycle selected from morpholinyl or piperidinyl optionally substituted with C<sub>1-4</sub>alkyl-, preferably methyl;

Het<sup>14</sup> represents morpholinyl;

-62-

Het<sup>16</sup> represents a heterocycle selected from morpholinyl or pyrrolidinyl;

Het<sup>20</sup> represents pyrrolidinyl or piperidinyl;

Ar<sup>4</sup> represents phenyl;

Ar<sup>5</sup> represents phenyl optionally substituted with cyano.

5

4. A compound according to any one of claims 1 to 3 wherein the R<sup>1</sup> substituent is at position 4', the R<sup>2</sup> substituent is at position 5' and the R<sup>3</sup> substituent at position 7 of the structure of formula (I).

10

5. A kinase inhibitor of formula (I).

6. A compound as claimed in any one of claims 1 to 4 for use as a medicine.

15

7. Use of a compound as claimed in any one of claims 1 to 4 in the manufacture of a medicament for treating cell proliferative disorders such as atherosclerosis, restenosis and cancer.

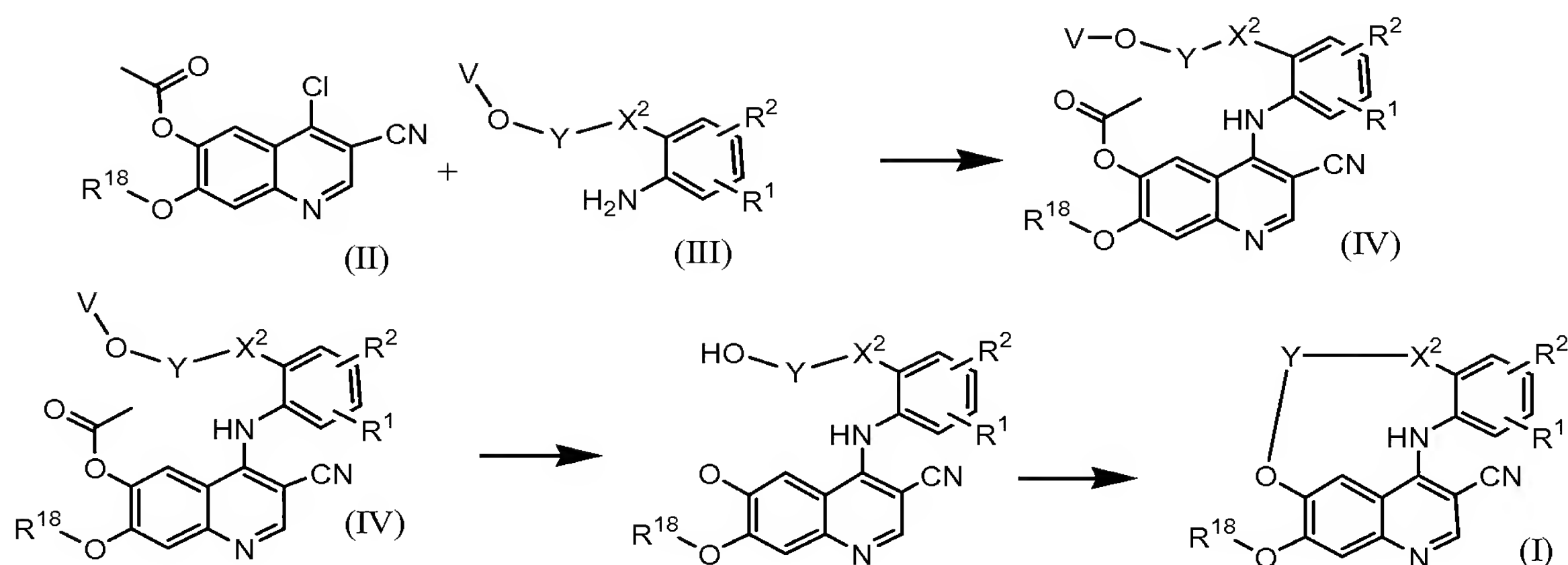
20

8. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and, as active ingredient, an effective kinase inhibitory amount of a compound as described in any one of the claims 1 to 4.

25

9. A process for preparing a compound as claimed in claims 1 to 4, comprising;  
a) coupling the known 6-acetoxy-4-chloro-3-cyano- quinolines of formula (II) with the suitable substituted anilines of formula (III) to furnish the intermediates of formula (IV), and deprotecting the intermediates of formula (IV) followed by ring closure under suitable conditions

-63-



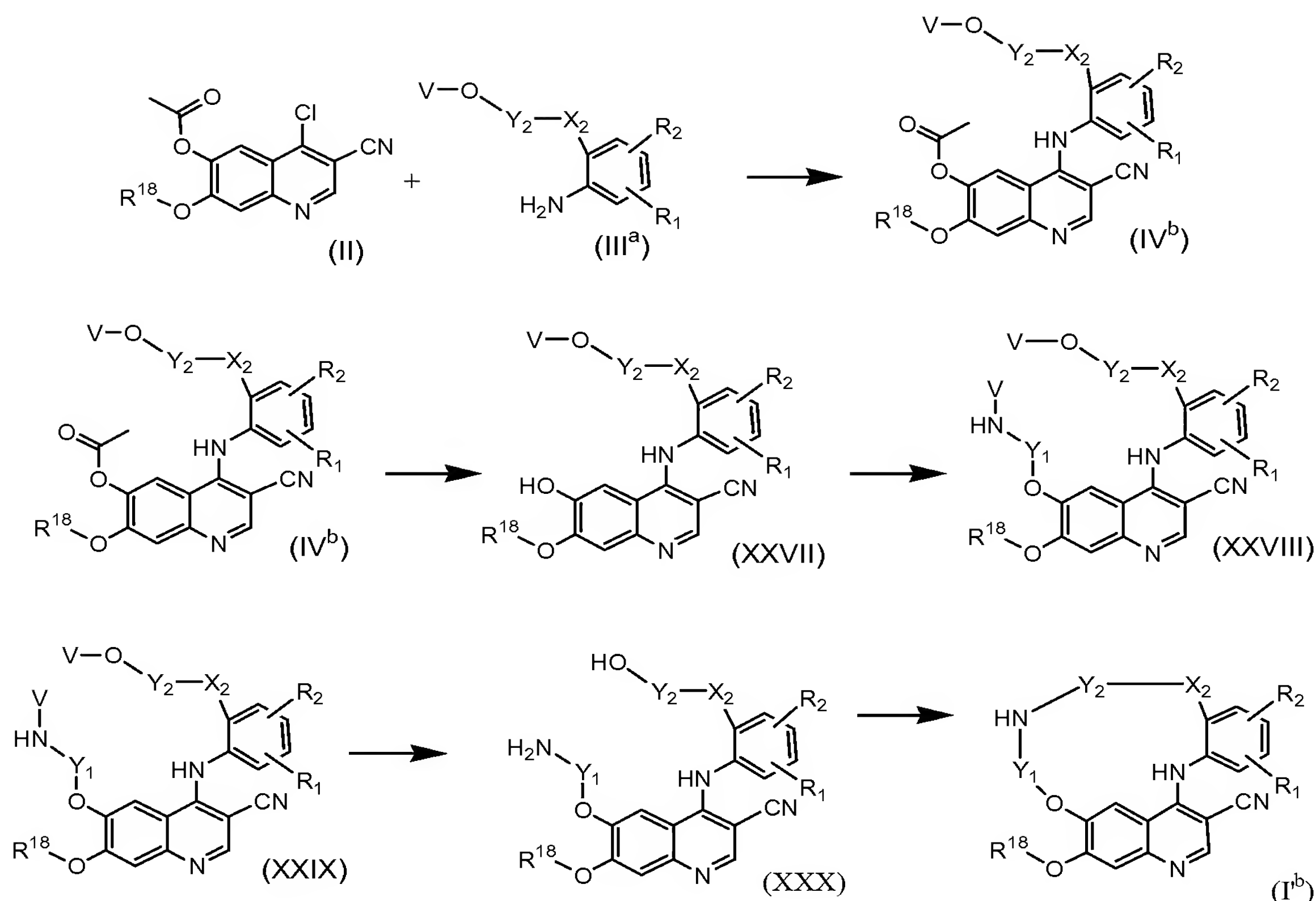
V = protective group such as for example methylcarbonyl, t-butyl, methyl, ethyl, benzyl or trialkylsilyl groups

R<sup>18</sup> represents Ar<sup>3</sup>, Ar<sup>4</sup>-C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkyl, C<sub>2-6</sub>alkenyl optionally substituted with Het<sup>12</sup> or R<sup>18</sup>

represents C<sub>1-4</sub>alkyl substituted with one or where possible two or more substituents selected from C<sub>1-4</sub>alkyloxy, hydroxy, halo, Het<sup>2</sup>, NR<sup>7</sup>R<sup>8</sup>, NR<sup>9</sup>R<sup>10</sup>-carbonyl or Het<sup>3</sup>-carbonyl, wherein Ar<sup>3</sup>, Ar<sup>4</sup>, Het<sup>12</sup>, Het<sup>2</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup> and Het<sup>3</sup> are defined as for the compounds of formula (I)

- 5 b) deprotection of the intermediates of formula (IV<sup>b</sup>) and subsequent formation of the corresponding ether using the appropriate aminated alcohol under standard conditions provides the intermediates of formula (XXVIII). Deprotection followed by ring closure provides the target compounds of formula (I'<sup>b</sup>).

-64-

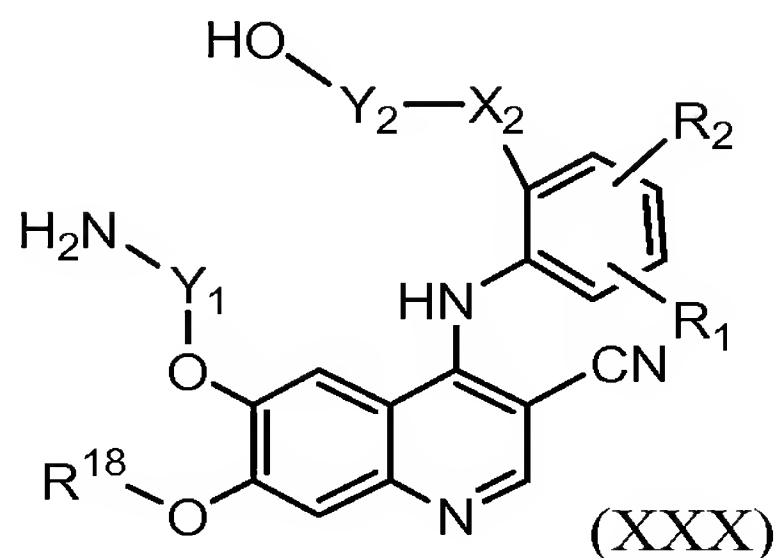


V = protective group such as for example, methylcarbonyl, t-butyl, methyl, ethyl, benzyl or trialkylsilyl groups, or in case of solid phase chemistry the resin to which the remainder of the molecule is attached

R<sup>18</sup> represents Ar<sup>3</sup>, Ar<sup>4</sup>-C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkyl, C<sub>2-6</sub>alkenyl optionally substituted with Het<sup>12</sup> or R<sup>18</sup> represents C<sub>1-4</sub>alkyl substituted with one or where possible two or more substituents selected from C<sub>1-4</sub>alkyloxy, hydroxy, halo, Het<sup>2</sup>, NR<sup>6</sup>R<sup>7</sup>, NR<sup>8</sup>R<sup>9</sup>-carbonyl or Het<sup>3</sup>-carbonyl, wherein Ar<sup>3</sup>, Ar<sup>4</sup>, Het<sup>12</sup>, Het<sup>2</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup> and Het<sup>3</sup> are defined as for the compounds of formula (I)  
Y<sub>1</sub> and Y<sub>2</sub> each independently represent a C<sub>1-5</sub>alkyl, CO-C<sub>1-5</sub>alkyl or CO-CH<sub>2</sub>R<sup>16</sup>-NH-

10. A method of treating a cell proliferative disorder, the method comprising administering to an animal in need of such treatment a therapeutically effective amount of a compound as claimed in any one of claims 1 to 4.

11. An intermediate of formula (XXX)



-65-

the pharmaceutically acceptable addition salts and the stereochemically isomeric forms thereof, wherein

$Y_1$  and  $Y_2$  each independently represent  $C_{1-5}$ alkyl,  $CO-C_{1-5}$ alkyl or  $CO-CH_2R^{15}-NH-$ ;

$X^1$  represents a direct bond, O,  $-O-C_{1-2}$ alkyl-, CO,  $-CO-C_{1-2}$ alkyl-,  $NR^{10}$ ,

5  $-NR^{10}-C_{1-2}$ alkyl-,  $-CH_2-$ ,  $-O-N=CH-$  or  $-C_{1-2}$ alkyl-;

$X^2$  represents a direct bond, O,  $-O-C_{1-2}$ alkyl-, CO,  $-CO-C_{1-2}$ alkyl-,  $NR^{11}$ ,

$-NR^{11}-C_{1-2}$ alkyl-,  $-CH_2-$ ,  $-O-N=CH-$  or  $C_{1-2}$ alkyl-;

$R^1$  represents hydrogen, cyano, halo, hydroxy, formyl,  $C_{1-6}$ alkoxy-,  $C_{1-6}$ alkyl-,

$C_{1-6}$ alkoxy- substituted with halo,

10  $C_{1-4}$ alkyl substituted with one or where possible two or more substituents selected from hydroxy or halo; and

$R^2$  represents hydrogen, cyano, halo, hydroxy, hydroxycarbonyl-,  $Het^{16}$ -carbonyl-,

$C_{1-4}$ alkyloxy carbonyl-,  $C_{1-4}$ alkyl carbonyl-, aminocarbonyl-,

mono- or di( $C_{1-4}$ alkyl)aminocarbonyl-,  $Het^1$ , formyl,  $C_{1-4}$ alkyl-,  $C_{2-6}$ alkynyl-,

15  $C_{3-6}$ cycloalkyl-,  $C_{3-6}$ cycloalkyloxy-,  $C_{1-6}$ alkoxy-,  $Ar^5$ ,  $Ar^1$ -oxy-, dihydroxyborane,  $C_{1-6}$ alkoxy- substituted with halo,

$C_{1-4}$ alkyl substituted with one or where possible two or more substituents selected from halo, hydroxy or  $NR^4R^5$ ,

$C_{1-4}$ alkyl carbonyl- wherein said  $C_{1-4}$ alkyl is optionally substituted with one or

20 where possible two or more substituents selected from hydroxy or  $C_{1-4}$ alkyl-oxy-;

$R^4$  and  $R^5$  are each independently selected from hydrogen or  $C_{1-4}$ alkyl;

$R^6$  and  $R^7$  are each independently selected from hydrogen,  $C_{1-4}$ alkyl,  $Het^8$ ,

aminosulfonyl-, mono- or di( $C_{1-4}$ alkyl)-aminosulfonyl, hydroxy- $C_{1-4}$ alkyl-,

25  $C_{1-4}$ alkyl-oxy- $C_{1-4}$ alkyl-, hydroxycarbonyl- $C_{1-4}$ alkyl-,  $C_{3-6}$ cycloalkyl,  $Het^9$ -carbonyl- $C_{1-4}$ alkyl-,  $Het^{10}$ -carbonyl-, polyhydroxy- $C_{1-4}$ alkyl-,  $Het^{11}$ - $C_{1-4}$ alkyl- or  $Ar^2$ - $C_{1-4}$ alkyl-;

$R^8$  and  $R^9$  are each independently selected from hydrogen,  $C_{1-4}$ alkyl,  $C_{3-6}$ cycloalkyl,  $Het^4$ , hydroxy- $C_{1-4}$ alkyl-,  $C_{1-4}$ alkyloxy- $C_{1-4}$ alkyl- or polyhydroxy- $C_{1-4}$ alkyl-;

30  $R^{10}$  represents hydrogen,  $C_{1-4}$ alkyl,  $C_{1-4}$ alkyl-oxy-carbonyl-,  $Het^{17}$ ,  $Het^{18}$ - $C_{1-4}$ alkyl-,  $C_{2-4}$ alkenyl carbonyl- optionally substituted with  $Het^{19}$ - $C_{1-4}$ alkylaminocarbonyl-,  $C_{2-4}$ alkenylsulfonyl-,  $C_{1-4}$ alkyloxy- $C_{1-4}$ alkyl- or phenyl optionally substituted with one or where possible two or more substituents selected from hydrogen, hydroxy, amino or  $C_{1-4}$ alkyloxy-;

35  $R^{11}$  represents hydrogen,  $C_{1-4}$ alkyl,  $Het^{13}$ ,  $Het^{14}$ - $C_{1-4}$ alkyl- or phenyl optionally substituted with one or where possible two or more substituents selected from hydrogen, hydroxy, amino or  $C_{1-4}$ alkyloxy-;

-66-

R<sup>15</sup> represents hydrogen or C<sub>1-4</sub>alkyl optionally substituted with phenyl, indolyl, methylsulfide, hydroxy, thiol, hydroxyphenyl, aminocarbonyl, hydroxycarbonyl, amine, imidazolyl or guanidino;

R<sup>18</sup> represents Ar<sup>3</sup>, Ar<sup>4</sup>-C<sub>1-4</sub>alkyl, C<sub>1-4</sub>alkyl, C<sub>2-6</sub>alkenyl optionally substituted with  
5 Het<sup>12</sup> or R<sup>18</sup> represents C<sub>1-4</sub>alkyl substituted with one or where possible two or more substituents selected from C<sub>1-4</sub>alkyloxy, hydroxy, halo, Het<sup>2</sup>, NR<sup>6</sup>R<sup>7</sup>, NR<sup>8</sup>R<sup>9</sup>-carbonyl or Het<sup>3</sup>-carbonyl;

Het<sup>1</sup> represents a heterocycle selected from piperidinyl, morpholinyl, piperazinyl, furanyl, pyrazolyl, dioxolanyl, thiazolyl, oxazolyl, imidazolyl, isoxazolyl,  
10 oxadiazolyl, pyridinyl or pyrrolidinyl wherein said Het<sup>1</sup> is optionally substituted amino, C<sub>1-4</sub>alkyl, hydroxy-C<sub>1-4</sub>alkyl-, phenyl, phenyl-C<sub>1-4</sub>alkyl-, C<sub>1-4</sub>alkyl-oxy-C<sub>1-4</sub>alkyl- mono- or di(C<sub>1-4</sub>alkyl)amino- or amino-carbonyl-;

Het<sup>2</sup> represents a heterocycle selected from morpholinyl, piperazinyl, piperidinyl, pyrrolidinyl, thiomorpholinyl or dithianyl wherein said Het<sup>2</sup> is optionally  
15 substituted with one or where possible two or more substituents selected from hydroxy, halo, amino, C<sub>1-4</sub>alkyl-, hydroxy-C<sub>1-4</sub>alkyl-, C<sub>1-4</sub>alkyl-oxy-C<sub>1-4</sub>alkyl-, hydroxy-C<sub>1-4</sub>alkyl-oxy-C<sub>1-4</sub>alkyl-, mono- or di(C<sub>1-4</sub>alkyl)amino-, mono- or di(C<sub>1-4</sub>alkyl)amino-C<sub>1-4</sub>alkyl-, aminoC<sub>1-4</sub>alkyl-, mono- or di(C<sub>1-4</sub>alkyl)amino-sulfonyl-, aminosulfonyl-;

Het<sup>3</sup>, Het<sup>4</sup> and Het<sup>8</sup> each independently represent a heterocycle selected from morpholinyl, piperazinyl, piperidinyl, furanyl, pyrazolyl, dioxolanyl, thiazolyl, oxazolyl, imidazolyl, isoxazolyl, oxadiazolyl, pyridinyl or pyrrolidinyl wherein  
20 said Het<sup>3</sup>, Het<sup>4</sup> or Het<sup>8</sup> is optionally substituted with one or where possible two or more substituents selected from hydroxy-, amino-, C<sub>1-4</sub>alkyl-, C<sub>3-6</sub>cycloalkyl-C<sub>1-4</sub>alkyl-, aminosulfonyl-, mono- or di(C<sub>1-4</sub>alkyl)aminosulfonyl or amino-C<sub>1-4</sub>alkyl-;

Het<sup>9</sup> and Het<sup>10</sup> each independently represent a heterocycle selected from furanyl, piperidinyl, morpholinyl, piperazinyl, pyrazolyl, dioxolanyl, thiazolyl, oxazolyl, imidazolyl, isoxazolyl, oxadiazolyl, pyridinyl or pyrrolidinyl wherein said Het<sup>9</sup> or  
30 Het<sup>10</sup> is optionally substituted C<sub>1-4</sub>alkyl, C<sub>3-6</sub>cycloalkyl-C<sub>1-4</sub>alkyl- or amino-C<sub>1-4</sub>alkyl-;

Het<sup>11</sup> represents a heterocycle selected from indolyl or  ;

Het<sup>12</sup> represents a heterocycle selected from morpholinyl, piperazinyl, piperidinyl, pyrrolidinyl, thiomorpholinyl or dithianyl wherein said Het<sup>12</sup> is optionally  
35 substituted with one or where possible two or more substituents selected from hydroxy, halo, amino, C<sub>1-4</sub>alkyl-, hydroxy-C<sub>1-4</sub>alkyl-, C<sub>1-4</sub>alkyl-oxy-C<sub>1-4</sub>alkyl-,

-67-

hydroxy-C<sub>1-4</sub>alkyl-oxy-C<sub>1-4</sub>alkyl-, mono- or di(C<sub>1-4</sub>alkyl)amino- or  
mono- or di(C<sub>1-4</sub>alkyl)amino-C<sub>1-4</sub>alkyl-;

Het<sup>13</sup> represent a heterocycle selected from pyrrolidinyl or piperidinyl wherein said  
Het<sup>13</sup> is optionally substituted with one or where possible two or more substituents  
5 selected from C<sub>1-4</sub>alkyl, C<sub>3-6</sub>cycloalkyl, hydroxy-C<sub>1-4</sub>alkyl-, C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyl  
or polyhydroxy-C<sub>1-4</sub>alkyl-;

Het<sup>14</sup> represent a heterocycle selected from morpholinyl, pyrrolidinyl, piperazinyl or  
piperidinyl wherein said Het<sup>14</sup> is optionally substituted with one or where possible  
two or more substituents selected from C<sub>1-4</sub>alkyl, C<sub>3-6</sub>cycloalkyl,  
10 hydroxy-C<sub>1-4</sub>alkyl-, C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyl or polyhydroxy-C<sub>1-4</sub>alkyl-;

Het<sup>16</sup> represent a heterocycle selected from morpholinyl, pyrrolidinyl, piperazinyl,  
1,3,2-dioxaborolane or piperidinyl wherein said heterocycle is optionally  
substituted with one or more substituents selected from C<sub>1-4</sub>alkyl; and

Het<sup>17</sup> represent a heterocycle selected from pyrrolidinyl or piperidinyl wherein said  
15 Het<sup>17</sup> is optionally substituted with one or where possible two or more substituents  
selected from C<sub>1-4</sub>alkyl, C<sub>3-6</sub>cycloalkyl, hydroxy-C<sub>1-4</sub>alkyl-, C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyl  
or polyhydroxy-C<sub>1-4</sub>alkyl-;

Het<sup>18</sup> and Het<sup>19</sup> each independently represent a heterocycle selected from morpholinyl,  
pyrrolidinyl, piperazinyl or piperidinyl wherein Het<sup>18</sup> and Het<sup>19</sup> are optionally  
20 substituted with one or where possible two or more substituents selected from  
C<sub>1-4</sub>alkyl, C<sub>3-6</sub>cycloalkyl, hydroxy-C<sub>1-4</sub>alkyl-, C<sub>1-4</sub>alkyloxyC<sub>1-4</sub>alkyl or  
polyhydroxy-C<sub>1-4</sub>alkyl-;

Ar<sup>1</sup>, Ar<sup>3</sup>, Ar<sup>4</sup> and Ar<sup>5</sup> each independently represent phenyl optionally substituted with  
cyano, C<sub>1-4</sub>alkylsulfonyl-, C<sub>1-4</sub>alkylsulfonylamino-, aminosulfonylamino-,  
25 hydroxy-C<sub>1-4</sub>alkyl, aminosulfonyl-, hydroxy-, C<sub>1-4</sub>alkyloxy- or C<sub>1-4</sub>alkyl.

12. Use of an intermediate of formula (XXX) in the synthesis of a compound of  
formula (I).